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Mini Review

Optic Nerve Head Hemangioblastoma; Manifestation and Treatment, a Mini-Review of Literature

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Abstract

Retinal hemangioblastoma is a benign vascular neoplasia which originates from neurosensory retina or optic disc. It might happen sporadically or be inherited dominantly manifesting as the constellation of systemic tumors which is called von Hippel Linadu disease. Optic nerve head hemangioblastoma is a subset of retinal hemangioblastoma which can present insidiously with subtle clinical manifestations. In this mini review, we evaluate the ocular manifestation of this disease. Additionally, we provide current treatment options for juxtapapillary retinal hemangioblastoma.

Keywords: *Retinal Hemangioblastoma (RH); von Hipple Lindau (VHL); Optic Nerve Head Hemangioblastoma*

Retinal hemangioblastoma (RH), also called retinal capillary hemangioma, retinal capillary hemangioblastoma, or retinal angioma, is a benign vascular neoplasia which originates from neurosensory retina or optic disc. RH typically occurs in the setting of von Hipple Lindau (VHL) disease which is an autosomal dominant disorder. Nonetheless, it can occur sporadically in the absence of VHL. Systemic involvement of VHL include Brain and spinal cord hemangioblastoma, renal cell carcinoma, pheochromocytoma, endolymphatic sac tumor, epididymal and broad ligament cystadenomas, pancreatic neuroendocrine tumors, renal and pancreatic cysts [1]. A better prognosis could be achieved by early diagnosis, surveillance, and treatment.

Diagnostic criteria of VHL includes a positive family history and presence of central nervous system hemangioblastoma, RH, clear cell carcinoma of kidney, or pheochromocytoma. In the absence of a positive family history two or more central nervous system hemangioblastoma or RH should be present. Additionally, one central nervous system hemangioblastoma or RH and a visceral tumor with the exception of ependymal and renal cysts (which are frequently observed in the general population) is sufficient.

Once the diagnosis of VHL is a concern in a patient a systemic work up is warranted to detect relevant lesions. Ophthalmoscopy begins from infancy and is repeated annually. A plasma or 24-hour urinary catecholamine level should be checked annually from 2 years or when the blood pressure is elevated. Yearly magnetic resonance imaging (MRI) of brain and spinal cord commence from age 11 years. Computed tomography (CT) or MRI of auditory canal and auditory tests should be requested with the onset of auditory loss, tinnitus, or vertigo. Eight years old patients should undergo ultrasonography of abdomen and CT scan of abdomen is indicated from 18 years old or earlier if clinically indicated.

Ocular involvement

Retinal Hemangioblastoma present unilaterally in 42% of cases and manifests exclusively in peripheral retina in 85% of eyes. Eight percent of tumors have proximity to optic disc and 7% have both juxtapapillary and retinal lesions. Only 33% of lesions are found in

ophthalmoscopy, while they showed other lesions using wide field angiography [2]. Additionally. 88% of tumors visualized by wide field angiography, are outside the standard fields of conventional fluoresceine angiography montage overlay. Beside this, WFA can detect more tumors in comparison with wide field color imaging [3]. Among 106 eyes of 55 patients with VHL, tumors were identified in 61.8% of cases using WFA. Fundus images could not detect 43 tumors (45.7%). Based on improved detection of RH with WFA, it is recommend to include periodic WFA images for early detection of small lesions.

Peripapillary tumors may be difficult to discern, presenting faintly as a fullness at neural rim of optic nerve head. Afferent and efferent vessels are typically absent; However, fine lacy vessels are appreciated on the surface of the tumor. They may be asymptomatic with gradual growth over years, but they eventually leads to exudative retinopathy. FA is crucial in diagnosis of juxtapapillary tumors which shows filling in the retinal arterial phase and diffuse hyperfluorescence and dye leakage in the late phase. It is presumed that deep optic nerve plexus and small superficial branches of the retinal arteries supply blood to the tumor.

One of the significant predictors of vision loss is increasing age. Additional risk factors are the concurrent presence of VHL disease, central or temporal location of the tumor, and the extension of the lesion. These lesions are variably vascular or fibrotic. They might regress spontaneously, be static, or become fibrotic and contractile. They may cause epiretinal membrane formation, when sufficiently near the fovea may decrease visual acuity. Retinal vascular proliferation occurs in 8% of eyes harboring RH [4]. This vasculopathy resembles retinal neovascularization seen in ischemic conditions; however, retinal capillary non-perfusion is generally absent.

Treatment

While the main goal of treatment in extrapapillary lesions is complete destruction of the tumor mass, there are some adverse consequences which can occur following ablative tumors near optic disc such as decrease in vision, altitudinal field defect, and development of central scotoma. Some tumors may be static for a long period of time. Additionally, exudation may remain stable and be associated with good visual acuity [5]. Variability in natural course and lack of efficacy of treatment to provide acceptable visual results have led to different therapeutic approach [6]. Laser photocoagulation for juxtapapillary RH is associated with permanent scotoma [7]. External radiation is also applicable for these tumors; however, proximity to optic nerve visual deterioration [7]. Current recommendation suggest observation of stable lesions. Photodynamic therapy has been advocated for symptomatic masses and seems to have better safety profile in comparison with photocoagulation and radiation therapy. In an interventional case series risk and benefits of PDT was assessed [8]. Five eyes suffering optic nerve head hemangioblastoma was treated with 6 mg/kg body surface area verteporfin followed by application of 100 j/cm^2 light at 692 nm. Patients received one to three courses of treatment until complete resolution of exudative retinopathy. Although treatment was successful in all patients, three eyes experienced 1, 3 and 10 line decrease in vision due to occlusion of retinal vessels or optic nerve ischemia.

Other treatment strategies have been suggested for juxtapapillary hemangioblastomas. Since the RCH shows elevated levels of vascular endothelial growth factor (VEGF), therefore anti-VEGF therapy may partake in treatment of these tumors [9]. It is speculated that hypoxia-induced factor produced by tumor cells leads to production of angiogenic factors [10]. Mennel., *et al*. reported a 44 year-old woman with decreased vision due to exudation in macula. Patient was treated with two sessions of PDT followed by 5 injections of intravitreal bevacizumab monthly. One year after therapy an increase in vision was evident and retinal structure restored to normal. They reported no adverse effect [11]. Another small case series reported outcome of three injection of intravitreal bevacizumab for 2 eyes with juxtapapillary hemangioblastomas. Vision improved from 20/80 to 20/20 in one patient, whereas the other eye did not show improvement [12]. In another case report successful treatment of JRH was achieved with combined PDT and intravitreal injection of ranibizumab [13].

Variability of treatment options and lack of large cohorts and randomized controlled trials preclude definite guideline for therapy. Risk of therapy should be judged weighing adverse effects, since the success rate is often limited.

Conclusion

Diagnosis of the optic nerve head hemangioblastoma require high level of suspicion and attention to meticulous signs of the tumor. Due to proximity to optic nerve head conventional destructive treatment is not a good option for this type tumor. Although observation is advised for asymptomatic stable tumors; PDT and anti VEGF therapy are among the armamentarium of treatment modalities which can be used in selected symptomatic patients.

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